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# Letters to the editor

## HEPATOTOXIC EFFECTS WITH HIGH-DOSE VENLAFAXINE

**DEAR EDITOR:**

Venlafaxine extended-release (VXR) is a novel, dual-acting serotonin-norepinephrine reuptake inhibitor (SNRI). It is commonly prescribed for major depression, as well as a variety of anxiety disorders, and belongs to the class of SNRIs that include duloxetine. Both medications block the reuptake of serotonin and norepinephrine; however, they do so with differing selectivity.[1] Although there have been recent alerts about the use of duloxetine in individuals with pre-existing hepatic disease, these particular warnings have not been extended to VXR.[2] We report the case of hepatic toxicity developing in an otherwise healthy patient whose bipolar depression was being treated with high-dose VXR. This case adds to at least three other reports in the literature that also document a potential hepatotoxic event associated with the use of VXR.[3–5]

**Case report.** Mr. H is a 33-year-old Caucasian man who has been followed in our clinic for nearly six years for treatment of his bipolar affective disorder. He recently presented for routine follow-up while being maintained on lithium carbonate, 600mg twice a day, quetiapine, 50mg at night, and VXR, 225mg/day. He had been taking the VXR at this dosage for six months after being maintained on 150mg/day for the previous six months. Immediately prior to increasing the dosage to 225mg/day, serum chemistries were obtained. The laboratory values were all within normal limits. Specifically, his alanine aminotransferase (ALT) had been 25IU/L (0–55) and his aspartate aminotransferase (AST) was 18IU/L (0–40).

On the day Mr. H was seen in our clinic, he reported a worsening depression over the course of four weeks, easy fatigue, excessive sleepiness during the day, and a lack of motivation. Along with obtaining a serum lithium level, which was normal, a comprehensive metabolic profile was ordered. These laboratory tests revealed an elevated ALT of 188IU/L and an AST of 215IU/L. Subsequent physical examination revealed abdominal and epigastric tenderness on palpation. A serum

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"Clinicians prescribing VXR should remain alert to the potential for hepatotoxic events in their patients and perhaps consider the use of routine liver enzyme monitoring in their ongoing care."

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hepatitis profile was negative for A, B, and C viral infections. Mr. H was taking only the medications prescribed and had no history of alcohol or illicit substance use.

A decision was made to lower the dosage of VXR to 150mg/day based upon the concern that he was experiencing a medication-induced hepatoxicity. We reasoned that lithium carbonate would be an unlikely cause of elevated liver enzymes due to its renal excretion and quetiapine had always been maintained at a very low dose throughout this person's treatment history. Moreover, when this individual had been taking lithium and quetiapine together with VXR at a dosage of 150mg/day for six months, his liver enzymes had been normal. The elevated liver enzymes and physical symptoms appeared over time only after titrating the VXR to 225mg/day.

Two weeks after reducing the VXR to 150mg/day repeat laboratory studies were obtained. Mr. H's ALT had decreased to 22IU/L and his AST was lowered to 23IU/L. He reported feeling physically improved since the lowering of the VXR dosage and had regained an appropriate level of energy, motivation and daytime alertness. He no longer complained of abdominal tenderness. However, he felt sadder and more depressed. He declined an increase in the VXR and, for obvious clinical and ethical reasons, was not rechallenged with the higher dosage. The VXR was tapered to discontinuation and lamotrigine was added to treat his bipolar depressive symptoms.

**Discussion.** The hepatotoxic effects of VXR have been attributed to an idiosyncratic reaction causing direct damage to the liver parenchymal cells.[6] This case is noteworthy given the increasing number of reports in the literature citing the potential association of toxic hepatic events with the use of VXR. Moreover, in our patient the toxic effects appeared to be dose-related since the physical symptoms of liver injury and abnormal laboratory values were temporally related to an increase in dosage from 150mg/day to 225mg/day. These findings subsequently normalized after the dosage was reduced from 225mg/day to 150mg/day.

As noted by others, clinicians prescribing VXR should remain alert to the potential for hepatotoxic events in their patients and perhaps consider the use of routine liver enzyme monitoring in their ongoing care.[3–5]

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With regards,


Richard C. Christensen, MD, MA
*Associate Professor, Director, Community Psychiatry Program, Department of Psychiatry, University of Florida College of Medicine*

Lorrie K. Garces, MD
*Fellow in Community Psychiatry, Department of Psychiatry, University of Florida College of Medicine*

Address correspondence to:
Richard Christensen, MD,
Department of Psychiatry,
University of Florida College of Medicine, 655 W. 8th Street
Jacksonville, FL 32209
Phone: (904) 244-3990
E-mail: richkchris@aol.com or richard.christensen@jax.ufl.edu